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The Efficacy of the 308 nm Excimer Laser in the Treatment of Psoriasis in Comparison to PUVA Therapy

Abstract

Background: Psoriasis is a common chronic inflammatory disorder associated with much physical and psychological comorbidity. There is currently no cure for psoriasis, and it is a disorder characterized by alternating periods of relapse and remission. The effectiveness of current treatments, such as psoralen UVA radiation therapy (PUVA), usually correlates with higher toxicity. Newer treatments that are effective, but less harmful are needed. The excimer laser is a newer treatment option for psoriasis that has shown promising effects. This review aims to determine the efficacy of the excimer laser compared to traditional PUVA therapy.

Methods: An exhaustive search of available medical literature was conducted using Medline-Ovid, CINAHL, Evidence-Based Medicine Reviews Multifile, and Web of Science using the keywords: *psoriasis*, *excimer laser*, and *PUVA therapy*. Relevant articles were then assessed for quality using GRADE.

Results: Two studies met inclusion criteria and were included in the systematic review. One randomized controlled trial of 272 patients with psoriasis demonstrated comparable effectiveness in elimination of psoriatic plaques between PUVA monotherapy and PUVA with additional excimer laser therapy. In addition, they determined that the combination group required fewer treatments and thus received a reduced cumulative UVA dose. Another small randomized controlled trial of 10 patients with palmoplantar psoriasis also demonstrated equal effectiveness of topical PUVA and excimer laser therapy.

Conclusion: The available data suggest that PUVA and excimer laser therapies offer similar effectiveness in clearing psoriatic lesions. However, there appear to be some inherent advantages to excimer laser therapy over PUVA monotherapy. When combined with PUVA therapy, the excimer laser decreases the number of treatments required for remission and therefore the total UVA dosage administered. The excimer laser also does not require additional medications to be taken prior to treatment. Further study is necessary to determine long-term efficacy and side effects of use, but currently this therapy appears promising as an option in the treatment of psoriasis.

Keywords: psoriasis, excimer laser, PUVA therapy

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Degree Name

Master of Science in Physician Assistant Studies

Keywords

psoriasis, excimer laser, PUVA therapy

Subject Categories

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The Efficacy of the 308 nm Excimer Laser in the Treatment of Psoriasis in Comparison to PUVA Therapy

Jocelyn Beth Lybarger



A Clinical Graduate Project Submitted to the Faculty of the

School of Physician Assistant Studies

Pacific University

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Faculty Advisor: Saje Davis-Risen, PA-C, MS

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Biography

Jocelyn Lybarger is a Nevada native. She received a Bachelor of Science degree in Nutritional Sciences with minors in Spanish and Psychology from the University of Nevada, Reno in 2010. After receiving her degree, she worked for a pharmaceutical research company in Reno, Nevada for two years prior to beginning PA school. She would like to pursue a career in dermatology or family medicine.

Abstract

Background: Psoriasis is a common chronic inflammatory disorder associated with much physical and psychological comorbidity. There is currently no cure for psoriasis, and it is a disorder characterized by alternating periods of relapse and remission. The effectiveness of current treatments, such as psoralen UVA radiation therapy (PUVA), usually correlates with higher toxicity. Newer treatments that are effective, but less harmful are needed. The excimer laser is a newer treatment option for psoriasis that has shown promising effects. This review aims to determine the efficacy of the excimer laser compared to traditional PUVA therapy.

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Figure I: Flow Diagram of Study Selection

List of Abbreviations

8-MOP.....	8-methoxypsoralen
BB-UVB.....	Broad-band ultraviolet B radiation
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
MED.....	Minimum erythema dose
MPD.....	Minimum phototoxic dose
NB-UVB.....	Narrow-band ultraviolet B radiation
PASI.....	Psoriasis Area and Severity Index
PUVA.....	Psoralen ultraviolet A radiation
UVA.....	Ultraviolet A radiation
UVB.....	Ultraviolet B radiation

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Appendix A.....	Psoriasis Area and Severity Index
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The Efficacy of the 308 nm Excimer Laser in the Treatment of Psoriasis in Comparison to PUVA Therapy

BACKGROUND

Psoriasis is a chronic inflammatory condition that affects about 2% of the population.¹ The pathophysiology of the condition is not completely understood, but it is generally accepted that it is characterized by keratinocyte over-proliferation, which has been linked to a substance that is produced by T lymphocytes.² This correlation is suggested by the fact that biopsies of skin affected by psoriasis have demonstrated proliferation and abnormal differentiation of keratinocytes, and infiltration of helper T-cells.³ As of yet, there is no cure for psoriasis and it is characterized by a pattern of relapse and remission. Depending on the severity and location, psoriasis can be very debilitating both physically and psychologically. For many patients, the erythema, scaling, and sloughing skin is a major cosmetic concern. The affected skin can also cause physical discomfort due to pruritic and/or painful lesions. When located on the hands and feet it can impair normal activities of daily living due to limited dexterity and mobility. Psoriasis has also been associated with an increased risk of depression, anxiety, and suicidal ideation.⁴ Other comorbidities associated with psoriasis include cardiovascular disease,⁵ psoriatic arthritis, lymphoma, inflammatory bowel disease, and non-alcoholic fatty liver disease.⁶

Moderate to severe psoriasis has traditionally been treated with narrow-band ultraviolet B radiation (NB-UVB) or psoralen UVA therapy (PUVA).⁷ Psoralen, usually in the form of 8-methoxypsoralen (8-MOP), is a photosensitizing agent that can be ingested or applied

topically via a cream or bath followed by UVA exposure. In this treatment, the entire skin area of the body, including affected and unaffected skin, is exposed to the UVA rays.

The excimer laser is a relatively new therapy that has demonstrated success in treating psoriasis.⁸ The laser emits focused UVB light with a wavelength of 308 nm by means of xenon chloride gas. Ultraviolet B radiation is effective in treating psoriasis due to its ability to reduce keratinocyte proliferation and cause T cell apoptosis.⁹ Unique to the excimer laser, it is administered via a hand-held device that has a spot diameter of 14-30 mm. This feature offers the advantage of only exposing the affected skin to UV radiation while sparing unaffected skin.¹⁰ Asawanonda et al¹¹ demonstrated that due to increased thickness, psoriatic plaques may withstand higher doses of UV radiation than the surrounding healthy skin. This allows for fewer treatments and a lower cumulative dose of UV radiation required to induce remission when compared to PUVA therapy.

The aim of this review is to determine the efficacy of the 308 nm excimer laser when compared to traditional PUVA therapy in the treatment of psoriasis.

METHODS

An exhaustive search of available medical literature was conducted using Medline-Ovid, CINAHL, Evidence-Based Medicine Reviews Multifile, and Web of Science using the keywords: *psoriasis*, *excimer laser*, and *PUVA therapy*. The search in Web of Science was further focused by excluding vitiligo from the search using “not.” Reference lists were also reviewed for additional relevant articles and the available studies were then limited to the English language and human studies. The abstracts were then assessed for relevance. Articles included in this

review included primary research that compared excimer laser therapy to PUVA therapy in patients with psoriasis. Articles were excluded that dealt primarily with pediatric populations and that lacked a comparative group (Figure I).

Relevant articles were then assessed for quality utilizing the Grading of Recommendations, Assessment, Development, and Evaluation system (GRADE).¹²

RESULTS

The initial search yielded 30 articles for review. After full article review, two randomized controlled trials^{13,14} were chosen that met inclusion criteria.

The first study by Trott et al¹³ was a randomized controlled trial that included 272 hospitalized patients with severe psoriasis affecting >20% of the body surface area. Participants were excluded if they had received systemic antipsoriatic treatment within the previous 4 months, had used topical treatments and/or other types of phototherapy within the previous 2 weeks, had concomitant or previous malignant skin tumors, or were under the age of 18. Of the 272 participants, there were 162 men and 110 women with a mean age of 50 years. The baseline demographic characteristics were similar between groups including the baseline Psoriasis Area and Severity Index score (PASI) (Appendix A). The control group of 123 patients received PUVA monotherapy orally or via bath 4 times a week for up to 6 weeks. Oral PUVA therapy consisted of ingesting 8-MOP two hours prior to UVA irradiation and bath PUVA was accomplished by soaking in 8-MOP for 20 minutes prior to irradiation. The initial UVA dose was determined based on skin type and the minimum phototoxic dose (MPD) that was

determined prior to treatment. The treatment group of 149 patients received PUVA therapy with up to 4 additional excimer laser treatment sessions during the first two weeks of therapy. An excimer laser generating monochromatic light on the wavelength of 308 nm was used. Initial doses were determined depending on the participants' skin types (I-VI). The dose was increased at the next treatment session if there was no significant erythema from the previous treatment. The outcomes measured were PASI reduction, cumulative UVA and UVB radiation doses, side effects, and reasons for discontinuing treatment. The PASI score was recorded by a non-blinded observer. Blinding was not feasible due to the multiple, small, focused areas of hyperpigmentation that were caused by the laser. The participants were further followed for 12 weeks to determine time to relapse.

Trott et al¹³ determined that both treatment and control groups attained notable reductions in PASI scores; however, there was no significant difference between the two groups in regards to the reduction. Of the 256 participants that completed therapy, 67.3% of the PUVA-only group and 63.6% of the PUVA/excimer group achieved complete clearance ($\geq 90\%$ reduction in PASI), 23.0% of the PUVA-only and 28.0% of the combination group reached partial clearance ($\geq 50\%$ reduction in PASI), and 9.7% of the PUVA-only and 8.4% of the combination group had slight improvement ($\leq 50\%$ reduction in PASI). In regards to the cumulative UVA dose, they learned that there was significantly reduced exposure in the PUVA/excimer group compared to PUVA monotherapy. In the PUVA-only group the cumulative dose was 53.2 ± 26.3 J/cm² while in the PUVA/excimer group it was 22.9 ± 5.8 J/cm². There was also a significant decrease in the number of treatment sessions and the total duration of therapy required to achieve clearance. The PUVA-only group required a mean of 27 ± 7 sessions over 6.5 weeks

while the PUVA/excimer group only required 15 ± 6 sessions over 4.2 weeks. A total of 16 participants (7 in PUVA-only and 9 in PUVA/excimer) dropped out due to inadequate time available for therapy. There were no drop-outs due to adverse side effects. The side effects that were observed were moderate erythema, hyperpigmentation, and blistering in both groups. During the 12 week follow-up period, fewer patients relapsed in the combination group versus the PUVA-only group (13 vs. 18), but it was not a significant difference.

The second study performed by Neumann et al¹⁴ was a randomized controlled trial with a left-right trial design. Ten participants with palmoplantar psoriasis were recruited (6 men and 4 women with a mean age of 47 years). Participants were excluded if they had used topical treatments within the past month, or if they had received photochemotherapy or systemic antipsoriatic treatment in the past. In this trial, each patient served as their own control and each was randomly assigned to receive cream PUVA on one side and excimer laser therapy on the contralateral side. On one side, psoralen was administered topically in cream form one hour before UVA irradiation, and on the contralateral side a 308 nm excimer laser was used after the minimum erythema dose (MED) was determined for each participant. The baseline right and left PASI scores were similar for each patient. Each treatment was performed 4 times per week for 5 weeks. The outcome measures that were evaluated were the PASI score, which was measured by a blinded investigator, and adverse side effects. This study determined that both groups achieved a statistically significant decrease in PASI scores; however, there was not a significant difference between the two groups. In the PUVA group, the mean initial PASI score was 26.3 ± 19.6 and reduced to 9.3 ± 9.43 after 5 weeks of treatment. In the excimer laser group, the mean initial PASI score was 28 ± 18.74 and decreased to 10.2 ± 12.2 after the fifth

week. The side effects noted were erythema in three patients treated with the excimer laser and erythema and skin irritation in four patients treated with PUVA therapy. The 12-week follow-up period yielded 1 patient who relapsed at both sites.

DISCUSSION

The available data from Trott et al¹³ and Neumann et al¹⁴ suggest that the use of the excimer laser in the treatment of psoriasis is as effective as PUVA therapy in clearing psoriatic plaques. However, it is difficult to ascertain the difference in efficacy between the two independent therapies from the information provided by Trott et al¹³ because the two therapies were not directly compared. Nevertheless, they were able to determine that the combination of the two therapies offers the advantage of leading to clearance of affected skin in a shorter amount of time, and with fewer treatments than PUVA monotherapy. This lessens the cumulative exposure to deeply penetrating and harmful UVA radiation. Prolonged use of PUVA monotherapy has been linked to an increased risk of squamous cell carcinoma due to the more vulnerable unaffected skin being exposed to UVA radiation. In a retrospective study by Lindelof et al,¹⁵ they determined that patients treated with PUVA therapy had a 5-fold (men) and 3-fold (women) increase in the incidence of squamous cell carcinoma. The average follow-up period was 16 years after PUVA therapy. Therefore, the combination therapy, with fewer treatments and lower UVA exposure, has the potential to result in a decreased risk of skin cancer, and provide increased patient satisfaction resulting in improved compliance with treatment.

Conversely, the study by Neumann et al¹⁴ directly compares the two therapies. The information from this study suggests that even though the two therapies appear to be equal in their effectiveness in clearing psoriatic lesions, excimer laser therapy is easier to perform and does not require the use of topical or oral photosensitizing agents which have been associated with several adverse side effects. Topical use of these medications has been associated with acute phototoxic dermatitis or pruritus. Systemic use can cause nausea and pruritus and also necessitates the use of skin and eye protection from sunlight during and for an extended period following treatment. Oral psoralen also carries a pregnancy category C rating¹⁶ and has been associated with an increase in low birth weight infants born to mothers who previously received systemic PUVA therapy.¹⁷ On the other hand, not much research is available regarding the use of the excimer laser and its safety during pregnancy. However, broadband UVB (BB-UVB) treatment is currently the treatment of choice in pregnancy for severe disease as long as overheating is avoided.¹⁸ The excimer laser also emits UVB radiation, but has the added advantage of being more localized than BB-UVB. This could be a starting point to support the laser's use in pregnant patients with psoriasis.

One factor that could potentially create biased results is the lack of blinding of investigators in the study by Trott et al.¹³ The investigators were recording the PASI scores as treatment progressed, and being aware of which treatment each patient was receiving creates the possibility of inadvertently altering the fairly subjective PASI score.

At this time, there is a need for larger randomized controlled trials comparing the excimer laser and PUVA therapy directly. The current research that was evaluated consists of a

fairly large study¹³ which did not compare PUVA and excimer laser therapy head-to-head, but as a combination therapy. The second study¹⁴ did compare PUVA and excimer directly, but had a very small population of only 10 patients. The current research on excimer laser therapy also lacks information regarding: adverse side effects associated with long-term use, long-term follow-up to determine duration of clearance, and relapse rates in comparison to other therapies. Presently, this long-term data is likely lacking due to the excimer laser being a somewhat new option in the treatment of psoriasis. See Table I.

While cost and insurance coverage are other aspects of patient care that must be considered when deciding on a treatment plan for a particular patient, the current data demonstrates a potential for the excimer laser to become a principal modality in the treatment of psoriasis.

CONCLUSION

To date, large randomized controlled trials evaluating the long-term effectiveness of the excimer laser compared to traditional PUVA therapy are lacking and further research is warranted. According to the GRADE criteria, the information gathered is of moderate quality due to the limitations discussed. Therefore, a weak recommendation can be made for the use of excimer therapy in the treatment of psoriasis. Nonetheless, due to the laser's ability to selectively target affected skin and the ease of administration, the excimer laser shows promise as a safer and easier to use alternative to PUVA therapy for the treatment of moderate to severe psoriasis.

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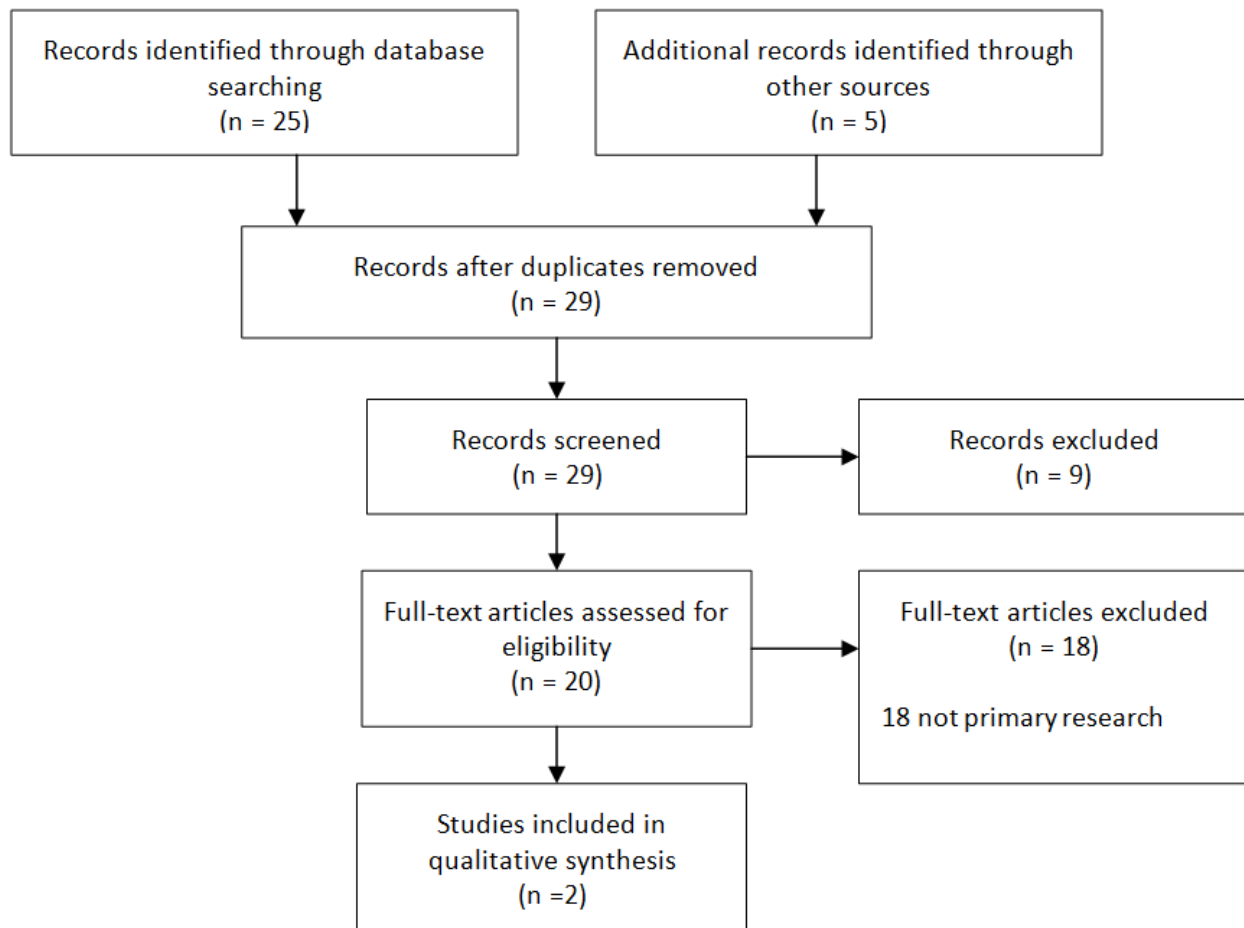
Table I. Characteristics of Reviewed Studies

Quality Assessment							
		Downgrade Criteria					Quality
Study	Design	Limitations	Indirectness	Imprecision	Inconsistency	Publication bias likely	
Trott et al ¹³	RCT	Serious limitations ^a	No serious indirectness	No serious imprecision	No serious inconsistencies	Not likely	Moderate
Neumann et al ¹⁴	RCT	Serious limitations ^a	No serious indirectness	Serious imprecision ^b	No serious inconsistencies	Not likely	Low

^aBoth studies lack patient allocation concealment, Trott et al¹³ also lacks blinding of investigator

^bSmall sample size of 10 participants

Figure I. Flow Diagram of Study Selection



Appendix A. Psoriasis Area and Severity Index (PASI)

The Psoriasis Area and Severity Index¹⁹ was developed as a standardized method of quantifying the severity and extent of a patient's psoriasis. The score ranges from 0-72 with higher scores indicating more severe disease.

Intensity and surface area are calculated for 4 body areas: head/neck, which is considered 10% of the body, arms (20%), trunk (30%), and legs (40%). Surface area is scored on a 7 point scale for each area: (0) 0%, (1) 1-9%, (2) 13-29%, (3) 30-49%, (4) 50-69%, (5) 70-89%, and (6) 90-100%. The intensity of erythema, induration, and desquamation are each rated on a 5 point scale for each of the 4 body areas: (0) none, (1) mild, (2) moderate, (3) severe, and (4) very severe.

E.g. Total body with most severe psoriasis:

Head: $6 (4+4+4) \times 10\% = 7.2$

Arms: $6 (4+4+4) \times 20\% = 14.4$

Trunk: $6 (4+4+4) \times 30\% = 21.6$

Legs: $6 (4+4+4) \times 40\% = + \underline{28.8}$

72